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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/341,505	07/12/99	JACKSON S	MEWE-005

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EXAMINER	
ROBINSON, H	
ART UNIT	**PAPER NUMBER**
1653	18

DATE MAILED: 09/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/341,505	Jackson et al.
Examiner	**Art Unit**
Hope Robinson	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 2, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-6, 19, 22, and 25* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6, 19, 22, and 25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Applicant's response to the Office Action mailed January 18, 2001 in Paper No. 17 on July 2, 2001 is acknowledged.

2. Claim 1-3, 5-6, 19, 22 and 25 has been amended. Claims 1-6, 19, 22 and 25 are pending.

3. The objections to the Specification and Oath/Declaration have been withdrawn. The following grounds of rejection are or remain applicable :

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-6, 19, 22 and 25 remain rejected under 35 U.S.C. 112 first paragraph, because the specification while being enabling for DNA dependent protein kinase (DNA-PK), DNA ligase IV and XRCC4, does not reasonably provide enablement for the fragment or variant thereof. Page 1 of the specification asserts that the invention relates to methods of screening, peptides,

mimetics and methods of use based on the discovery and characterization of an interaction between known proteins and that these interactions play a key role in DNA repair. The protein in question are XRCC4 and DNA ligase IV. In addition, page 4 of the specification asserts that "the present inventors have shown that XRCC4 exists ... and demonstrated convincingly that it interacts with DNA ligase IV and also DNA-PKcs/Ku". Does the fact that XRCC4 interacts with the above protein give it a function? Further, the specification at page 6 indicates that the physiological function of mammalian ligase IV is unknown. Additionally, the specification on page 7 asserts that XRCC4 was known to be involved somehow in Ku-associated DNA double stranded break repair (KADR) but its biological activity was obscure, thus the present invention established for the first time the biological activity of XRCC4, that is binding to DNA ligase IV. However, the mere binding activity does not disclose a specific function for the protein XRCC4, especially since the specification discloses that a clear function for DNA ligase IV has not been flattened by science.

Although the specification asserts that the present invention has discovered that DNA ligase IV is important for double strand DNA break repair via non-homologous end joining (NHEJ). The specification does not provide any convincing evidence/data of the asserted function, nor any detail as to what the "strong interaction" between XRCC4 and DNA ligase IV involves nor what the "modulation of the interaction between XRCC4/DNA ligase IV and between XRCC4/DNA-PKcs/Ku entails (see pages 7-9). Additionally, the claims broadly recite

"an assay method for an agent which modulates the binding between XRCC4 and DNA ligase IV etc., however, there is no indication in the claims whether "modulation" is upward or downward.

Furthermore, the specification on pages 15+ discloses that suitable fragments of XRCC4 or DNA ligase IV include those which include residues which interact with the counterpart protein. Further, smaller fragments, analogues and variants of this fragment may be similarly employed. Such peptide fragment are obtainable by means of deletion analysis and/or alanine scanning of the relevant protein making an appropriate mutation in sequence. Further, the specification provides a superficial discussion on derivatives, variants and analogues. Clearly, this description is lacking the size/type of fragment, and does not provide any features related to a derivative, variant or analogue commensurate in scope with the claims.

Moreover, no substantive guidance/direction is given regarding the claimed assay method, how to find a test compound, how much XRCC4 is included, is modulation up or down, how is the interaction determined and no proper measuring steps are provided. See for example, on page 28, where the specification asserts that "precise format of an assay of the invention may be varied by those of skill in the art using routine skill and knowledge". An example is then provided of an "in vitro labeling study". However, this discussion is not limiting and does not breathe life into the claims, especially since the claimed invention is directed to "an assay method".

Absent exemplification of a specific assay to assay a specific compound the specification is not enabled for an "assay method" as claimed. Further, since no guidance or direction is provided regarding the test compound, the derivative, variant or analogue thereof, for DNA ligase IV,

XRCC4 and DNA-PKcs/Ku it would require undue experimentation to be able to practice the claimed invention.

Thus, for all of the above reasons, the specification is not considered to be enabling without undue experimentation, because, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to enable one skilled in the art to be able to practice the invention commensurate in scope with these claims.

5. Applicant's arguments filed July 2, 2001 in Paper No. 17 has been considered, however, the rejection under 35 U.S.C. 112, first paragraph remains. Applicant's response contends that the terms fragment and variant have not been removed as they are fully enabled to a person of ordinary skill and are important in providing a scope of protection commensurate with the contribution of the present invention to the art. Further, it is argued that a skilled person is able to make fragments of a full length polypeptide or sequence variants without undue experimental exertion. However, neither the claims nor the specification provide the size or function or describe any special features of the fragments and variants commensurate in scope with the claims.

Applicant's response also contends that the present application teaches for the first time the binding of XRCC4 with DNA ligase IV and DNA-PKcs, however, the claims are not directed with particularity to binding of XRCC4 with DNA ligase IV and DNA-PKcs, but instead are directed to an assay method for an agent which modulates the binding between XRCC4 and DNA

ligase IV, or XRCC4 and DNA-Pkcs/Ku, or XRCC4, DNA ligase IV and DNA-PKu comprising (i) and (ii) described in claim 1, for example. Therefore, this argument is not convincing. Applicant further contends that the interaction (i.e. binding) between molecules has been fully characterized in the specification. However, the claims recite "modulates the binding" and modulation can be defined as increased or decreased , enhanced or diminished or interrupts or inhibits, thus the interaction has not been clearly characterized. Note also that the response on page 6 states that "agents identified by the present methods which reduce or increase the binding of these components of the KADR apparatus are useful as modulators of the operation of the KADR pathway and therefore as potential therapeutics. These assay methods can be used to obtain suitable agents without any further elucidation of the mechanisms of KADR". If they bind tightly as stated (see also pages 7-9 of the specification), why then would applicant want to increase binding, what can be achieved?

Furthermore the response on page 7 argues that the invention is not limited to any particular assay format, however, various assay methods and formats are described at length in the application. How is one of ordinary skill in the art to determine the format without undue experimentation based on the present disclosure? Which one of the assay methods is to be applied commensurate in scope with the claims? As the specification lacks exemplification of a specific assay to assay a specific compound the specification is not enabled for an "assay method" as claimed. Further, since no guidance or direction is provided regarding the test compound, the derivative, variant or analogue thereof, for DNA ligase IV, XRCC4 and DNA-PKcs/Ku it would

require undue experimentation to be able to practice the claimed invention. Therefore, for the reasons stated above the rejection has been maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6, 19, 22 and 25 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Amended claim 1 is indefinite because the claim recites "an agent", "a substance" and "a compound", and the terms are inconsistent (see for example the preamble which recites "an agent which modulates"; (i) which recites "bringing into contact a substance", (ii) which recites "a test compound" and the end of the claim which recites "reduction or abolition in binding between said substances" (see also claim 2). The claim is also indefinite for the recitation of " modulates", does modulation mean inhibition or activation, increase or decrease (see also claims 2, 3, 19, 22 and 25). The claim has been amended to include the typical markush language of "selected from the group consisting of", however, the claim represents an improper markush as the listing consists of several "or". Note that a proper markush listing consists of "A, B, C or D or A, B, C, and D. The dependent claims are also included in this rejection.

Claim 3 is indefinite because the claim recites "determining DNA ligase activity in the presence an absence of test compound, a **difference in activity** in the presence relative to the **absence of test compound**". Note that the article "the" is missing between "the phrase "absence of test compound"and the claim does not provide any information as to what the "difference" is (see also claim 6). The dependent claims are also included in this rejection.

Amended claim 5 is indefinite because the claim recites "determining adenylation or labeling" without reciting how the determination will occur. Positive method steps delimiting how this use is actually practiced is necessary. The claim is further indefinite as to "end-joining of strands" what are "end-joining"? The claim also remains indefinite as to the recitation of analogues without describing any special features of the analogues.

Claim 6 remains indefinite because the claim recites "peptide fragments and variants" without any recitation of the characteristics of the fragments or variants. In addition, the claim is indefinite because the word "including" is recited because there is no indication of how much of the substance, agent or compound is included (see also claims 19, 22 and 25).

7. Applicant's arguments filed July 2, 2001 in Paper No. 17 has been considered, however, the rejection under 35 U.S.C. 112, second paragraph remains. Applicant's response contends that claim 1 has been amended to relate binding to modulating, however, the degree of modulation (i.e., upwards or downwards) has not been set forth. Further, the response asserts that the

invention relates to the characterization of novel interactions, not to a method of determining the interaction between proteins. This argument is not convincing as the claims are directed to an assay method. Applicant also contends that claim 1 has been amended to recite an agent, however, this appears to be inconsistent with the recitation of "a compound" and " a substance" in the same claim. Additionally, applicant did not delete the terms fragment or variant from the claims as these terms were deemed definite, however, as no special feature has been described the claims remain indefinite. Furthermore, applicant argues that the term "including" has been deleted from the claims, however, as noted above it still appears in several claims. Note also that new grounds of rejection under 35 U.S.C. 112, second paragraph has been instituted based on applicant's amendments to the claims. Therefore, for the reasons stated above the rejection has been maintained.

Conclusion

8. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The examiner can normally be reached on Monday and Wednesday-Friday from 9:00 am to 5:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response.

The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope Robinson, MS

Patent Examiner

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER